EXHIBIT C

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 5 Cases*	

EXPERT REPORT OF MARSHALL SHOEMAKER, M.D.

I. INTRODUCTION

A. This report contains my opinions regarding the design, safety, and efficacy of the Gynecare TVT, TVT-O, TVT Abbrevo and TVT Exact midurethral slings. It is my opinion that all these products are safe and effective and provided adequate warnings and instructions to doctors. This report will also contain a summary of my qualifications, training, education, and experience from which I base my opinions. I have reviewed and considered published medical literature and literature reviews, journal articles, textbooks, and materials provided to me by Counsel for Ethicon and Johnson & Johnson (including company documents, reports and depositions of plaintiff experts, discussed therein). I also have materials which I have reviewed as a preceptor for Gynecare throughout the years. The materials that support these opinions will be in my reference list. I do hold that these opinions are within a reasonable degree of medical certainty, and if I receive additional information prior to trial, I reserve the right to add or change my opinions.

B. I am currently being paid $500 an hour to prepare a written report and review literature and $700 an hour for depositions.

II. BACKGROUND.

A. My name is Marshall D. Shoemaker, MD. I attended the University of Alabama and graduated with a Bachelor of Science in Biology in 1979. I am Board Certified in Obstetrics and Gynecology and attended Texas Tech School of Medicine from 1979 to 1983. I did my residency at Parkland Memorial Hospital with The University of Texas Southwestern Medical School in Dallas from 1983 to 1987. I was chief resident in my fourth year of residency and was voted “Outstanding Resident” for 1987 by my peers. I joined a group of Parkland residents in a private practice in Corpus Christi, Texas

from 1987 until 1997. We were on the cutting edge of gynecological surgery and in the mid-1990s we were doing laparoscopic Burch procedures with mesh. Within my group, several of us were interested in pelvic floor repair and went to cadaver labs with emphasis in pelvic anatomy. We were doing open uterosacral suspensions with paravaginal repairs and Burch procedures until I moved to Fairhope, Alabama, in 1998. At that time, I realized there was no one in our area who was interested in pelvic floor repair, although there was a large patient population with pelvic organ prolapse and incontinence. I continued with the open procedures until the year 2000, when I became the first gynecologist in lower Alabama to do a classic transvaginal tape urethropexy (retropubic).

Specific to the treatment of SUI (Stress Urinary Incontinence), I have utilized various nonsurgical treatments including prescription antibiotics to treat urinary tract infections, anticholinergic medicines to treat overactive bladder, and pelvic floor exercises with specified physical therapy. I first learned the Marshall-Marchetti-Krantz (MMK) procedure, followed by a simple anterior repair with bladder neck suspension (Kelly plication). Next was the Burch procedure (both open and laparoscopic), the pubovaginal sling procedure using autologous rectus fascia, and the midurethral sling procedure utilizing synthetic mesh, which is now considered the gold and current standard of care for surgically treating stress urinary incontinence. In 2004, I became a preceptor for Ethicon for pelvic floor mesh and sling procedures. I have done approximately 1,300 sling procedures including retropubic, transobturator, and single site procedures using synthetic mesh from several different sling companies. The overwhelming majority of procedures, however, were using Ethicon's products, TVT and TVT-O.

I am well aware of the development of the surgical procedures, which have evolved over time, to treat stress incontinence. I am also mindful of the importance of the

polypropylene mesh, which was used by physicians seeking a more effective treatment of stress urinary incontinence. The surgical procedures as well as the use of the polypropylene mesh have had a significant impact on the lives of my patients. I have implanted Ethicon's mesh products, which are both laser-cut and mechanically cut, and have never seen a difference between the two products. In my experience, there has been no difference in the two types of mesh employed in the rates of erosion, exposure, extrusion, and dyspareunia in my patients. It is my opinion that midurethral slings are currently considered the gold standard for the treatment of stress urinary incontinence and is supported by published literature, metaanalysis, systemic reviews, published opinion statements, and practice guidelines of numerous organizations specializing in the treatment of urological and gynecological treatments. These publications include AUGS, AUA, SUFU, IUGA, NICE, AAGL, EAU, and ACOG. These organizations are highly regarded and respected in this specialized field of medicine. I currently use Ethicon's TVT Exact (retropubic), TVT-O (Abbrevo), and the Coloplast Altis, as a single-incision alternative to full-length midurethral slings.

III. URINARY INCONTINENCE

A. Background

1. Urinary incontinence is the involuntary leakage of urine and is a common condition in women, particularly as they age. It may result from many different abnormalities, including pelvic floor dysfunction and abnormalities in the lower urinary tract. As an example, stress urinary incontinence (SUI) occurs with physical exertion, such as lifting, bending, coughing, sneezing, or other activities or movement. Urgency incontinence occurs in the setting of bladder muscle contraction causing a sudden need to urinate, resulting in an involuntary urine leakage. Mixed urinary incontinence includes both SUI and urgency incontinence at different percentages. For example, women's incontinence may be 75% stress incontinence and 25% overactive bladder and all various percentages in between.

All of these conditions have a debilitating effect on women, both physically and emotionally, and can significantly affect the women's quality of life. Many women limit their social activities and relationships because of fear of embarrassment. Incontinence can also impact women economically by impeding their ability to perform occupational tasks because of a need to be near a bathroom. It may have a significant effect on sexual function resulting in a woman's not participating in sexual activity because of either incontinence during sex or fear that incontinence will occur.

B. Stress urinary incontinence (SUI)

1. Stress urinary incontinence is a common condition in women. The prevalence of incontinence increases with age and is a major public health concern as our population ages. In the nonelderly population, the expectation of cure has increased the utilization of a surgical approach.[1] SUI is defined by the involuntary loss of urine during effort and activity associated with increased intra-abdominal pressure. The lifetime risk for a female is increased with physical trauma and denervation of vaginal delivery. Nonsurgical approaches are available but are limited by the lack of qualified providers and the gap in knowledge of evidence-based protocols.[2,3] Mid urethral slings have been compared against pelvic floor behavioral therapy, and the slings have been found to have a superior cure rate.[4] The lifetime risk of a woman requiring stress incontinence surgery is 13.6%.[5] The

[1] Nygaard I, et al., Prevalence of Symptomatic Pelvic Floor Disorders in US Women. JAMA 2008;300(11):1311-16.
[2] McBride A, Pathophysiology of Stress Incontinence, J Pelvic Med 2004 Jan/Feb.
[3] Starr, JA, *The Female Pelvic Reconstruction Surgery* (2013, September/October)
[4] Labrie J, et al., Surgery versus physiotherapy for stress urinary incontinence. N Engl J Med 2013 Sep 19;369(12):1124-33.
[5] Wu JM, et al., Lifetime Risk of Stress Incontinence or Pelvic Organ Prolapse Surgery. Obstet Gynecol 2014 Jun;123(6):1201-6.

number of surgical procedures for stress urinary incontinence has increased from 37,953 in 1998 to 94,910 in 2007.[6]

The surgical option for treating stress urinary incontinence has been proven repeatedly with multiple studies and excellent clinical data. Historically, there are multiple surgical procedures that have been employed to treat stress urinary incontinence. These procedures evolved over time as physicians constantly sought to find more effective procedures to treat this very troublesome condition. Prior to the last decade, SUI was treated with procedures such as the MMK, anterior colporrhaphy, and needle suspension procedures. Their use declined as more innovative and effective treatments evolved and were recommended by the medical associations as they largely dictate current standards of care. SUI has been treated more recently with Burch colposuspension, autologous fascial slings, and most often with synthetic slings. No surgical treatments for stress incontinence are without risks. The following commonly known risks include:

- damaged organs like the bladder
- ureteral injury
- damage to bowel
- damage to vessels
- damage to nerves
- anesthesia risks
- wound complications requiring intervention
- infection
- incisional hernia
- seroma or hematoma

[6] Wu JM, et al., Trends in inpatient urinary incontinence surgery in the USA, 1998-2007. Int Urogynecol J 2011 Nov;22(11):1437-43.

- granulation tissue or stitch granulations
- bleeding
- need for blood transfusion
- DVT
- Fistula
- recurrent urinary tract infection
- need for repeat surgery
- current cystitis
- catheter complications
- voiding dysfunctions
- de novo detrusor overactivity
- urinary retention
- urinary frequency
- need for self-catheterization
- persistent voiding dysfunction
- pain
- pain in the groin
- dyspareunia
- ileus or a bowel obstruction

The only unique risk for the use of pelvic mesh, however, is the risk of mesh erosion, exposure, or extrusion.[7] All pelvic surgeons are trained in their residencies to treat SUI. These risks from these surgeries are all well established, and physicians are aware of the risks during training.[8] These risks are continually

[7] FDA March 27, 2013, Position Statement Consideration about Surgical Mesh for SUI, AUA October 2013 Position Statement on The Use of Vaginal Mesh for the Surgical Treatment of Stress Incontinence.

[8] American Board of Obstetrics and Gynecology, Inc., Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery 2012 (fellows will discuss the alternatives, risks, benefits,

addressed in the published literature, and all pelvic surgeons are required to participate in continuing medical education to maintain active licenses and credentials. These risks are second nature to pelvic reconstructive surgeons, and physicians are well aware of potential complications and, therefore, may not be included in professional materials or IFUs for the TVT family of products.

C. Ethicon's TVT line products

1. Development

Ethicon's TVT line of products is comprised of knitted, lightweight, monofilament, large-pore (macroporous) Prolene polypropylene, the most common type of synthetic material used in sling procedures. This material has the longest track record of safe and effective use. Permanent Prolene polypropylene sutures have been used safely in patients for many decades in all types of surgery with little or no reported problems with suture material, such as degrading, particle loss, enhanced scarring, excessive foreign body reaction, cytotoxicity, or increased infection rates. Synthetic polypropylene mesh has also been safely and effectively used for decades in various abdominal procedures. In the early 1990s, Dr. Ulmsten and his colleagues sought to improve the outcomes of their surgical treatments of SUI. Prior to that time, much of the surgical treatment was focused on providing enhanced support to the bladder neck. This surgery was invasive and not as

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complications, success rates, and levels of evidence for various surgical treatments of pelvic organ prolapse, including vaginal mesh procedures); AUGS Resident Learning Objectives (residents should understand the possible complications of surgical correction of pelvic organ prolapse and be able to counsel the patient on treatment plan, including side-effects, risk, failure, and complications); Accreditation Council for Graduate Medical Education Program Requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery Pt. IV.A.5.b).(2).(c) (fellows completing the F2 year must demonstrate competence in their knowledge of contraindications, limitations, indications, complications, techniques, and interpretation of results of screening, diagnostic, and therapeutic procedures including surgery for pelvic organ prolapse and urinary incontinence).

effective as Dr. Ulmsten and his colleagues desired. They began using a sling made of synthetic polypropylene which revolutionized incontinence surgery because the sling was implanted at the mid urethra rather than at the bladder neck. Their efforts resulted in the development of the TVT retropubic sling.[9,10] Given the minimally invasive nature of the TVT, its technical simplicity, the consistency of the product, and the high efficacy without the risk of major abdominal incision, TVT eventually became the gold standard to incontinence surgeons in the USA.[11] The placement of a nonabsorbable macroporous polypropylene tension-free synthetic sling under the mid urethra is the current standard for the treatment for female stress incontinence. The type 1 polypropylene mesh, and in particular, the Prolene polypropylene mesh, used in TVT has the highest biocompatibility when used to treat stress incontinence and is used predominantly in each current clinical practice.[12]

2. TVT and TVT-O

In 1998, the FDA cleared the TVT, which was the first midurethral sling used in Prolene polypropylene without stitching or anchoring to supporting tissue or bone. The technique was novel in the avoidance of the tension provided by an anchoring suture or bony attachment, placement at the mid urethra, and the use of a synthetic material. However, the configuration of the sling placement and the passage of needles through the space of Retzius were well-established by the use of previous

[9] Petros, PE, Creating A Gold Standard Surgical Device, *International Urogynecology* (2015)
[10] Falkener, C, et. al., Influence of Different Sling Materials on Connective Tissue Metabolism, *International Urogynecology of Pelvic Floor* (2001)
[11] Serati M, et al., Surgical treatment for female stress urinary incontinence: what is the gold-standard procedure? Int Urogynecol J 2009;20:619-21; Cox A, et al., Surgical management of female SUI: is there a gold standard? Nature 2013;10:78-89.
[12] Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375. DOI: 10.1002/14651858.CD006375.pub3

pubourethral slings. The monofilament macroporous Prolene polypropylene demonstrated useful attributes, tolerability, and a long history of use as both mesh and suture.[13] Placement of the sling at the mid urethra was conformed to the newly acquired knowledge of the continence mechanism.[14] The TVT is a mid-urethral sling which is implanted intravaginally using a retropubic approach. The TVT mesh is attached to a needle which is inserted into the vagina through a small (about 1.5 cm) incision, creating a mid-urethral sling effect. The needles are passed through the vagina, essentially scraping the back of the pubic bone and exiting the lower abdomen. It is placed without tension to support the midportion of the urethra. Cystoscopy is required during the procedure to ensure there is no bladder injury. Intravaginal stress incontinence surgery using a mesh sling is minimally invasive. It is a much quicker procedure and uses minimal anesthesia, which also represents less recovery time, as well as less time away from work and other activities. In 2001, the five-year data on the use of full-length TVT surpassed the cure rates for previously used continence procedures.[15] Cure rates beyond 80% were consistently reproduced, being commonly reported, and results of randomized controlled trials (RCTs) were reported in 2002. The highest level of scientific evidence showed TVT to be equally effective to Burch procedures.[16] With the widespread use of TVT as the primary incontinence procedure, an unprecedented quality and amount of outcome data became available to surgeons.

[13] Falconer C, Influence of Different Sling Materials on Connective Tissue Metabolism in Stress Urinary Incontinent Women. Int Urogynecol J 2001 (Suppl 2):S19-23.
[14] Petros PE, An Integral Theory and its Method for the Diagnosis and Management of Female Urinary Incontinence. Scand J Urol Nephrol. 1993 (Suppl. No. 153).; Ulmsten U, et al., An Ambulatory Surgical Procedure Under Local Anesthesia for Treatment of Female Urinary Incontinence. Int Urogynecol J 1996;7:81-86.
[15] Nilsson CG, et al., Long-term Results of the Tension-Free Vaginal Tape (TVT) Procedure for Surgical Treatment of Female Stress Urinary Incontinence. Int Urogynecol J 2001(Suppl 2):S5-S8.
[16] Ward K and Hilton P, Prospective multicenter randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. BMJ 2002;325:67.

Scrutiny over efficacy and safety became the subject of multiple publications with confirmation of consistent efficacy and reproducibility over previously used procedures. TVT and TVT-O data has been reported in all levels of evidence into a depth not previously recorded for any known incontinence procedure.[17]

Delorme described the placement of a midurethral sling with a transobturator approach by placing insertion needles from the outside in.[18] Dr. de Leval described

[17] Nilsson CG, Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. Int Urogynecol J 2008;19:1043-1047; Liapis A, Long-term efficacy of tension-free vaginal tape in the management of stress urinary incontinence in women: efficacy at 5 and 7 year follow-up. Int Urogynecol J 2008;19:1509-1512; Olsson I, et al., Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence, Int Urogynecol J 2010;21:679-683; Aigmueller T, et al., Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol 2011 Nov;205(5):496.e1-5; Groutz A, et al., Ten-Year Subjective Outcome Results of the Retropubic Tension-Free Vaginal Tape for Treatment of Stress Urinary Incontinence. J Minim Invasive Gynecol 2011;18:726-29; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol 2012 Nov;19(11):1003-9; Serati M, Tension-free Vaginal Tape for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 10-Year Follow-Up, European Urology 2012;61:939-946; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J 2013 Aug;24(8):1271-8; Nilsson CJ, Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J, 2013 Aug;24(8):1265-9; Serati M, et al., TVT for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 13-Year Follow-Up. Neurourol Urodyn 2017 Jan;36(1):192-7 Novara G, et al., Tension-Free Midurethral Slings in the Treatment of Female Stress Urinary Incontinence: A Systematic Review and Meta-analysis of Randomized Controlled Trials of Effectiveness. Eur Urol 2007;52:663-79; Novara G, et al., Complication Rates of Tension-Free Midurethral Slings in the Treatment of Female Stress Urinary Incontinence: A Systematic Review and Meta-Analysis of Randomized Controlled Trials Comparing Tension-Free Midurethral Tapes to Other Surgical Procedures and Different Devices. Eur Urol 2008;53:288-309.

[18] Delorme E, Trans-obturator tape: a mini invasive procedure for the treatment of female stress urinary incontinence. Progrès en Urologie 2001; Delorme E, et al., Transobturator Tape (Uratape): A New Minimally-Invasive Procedure to Treat Female Urinary Incontinence. Eur Urol 2004;45:203-07.

an approach by inserting the needles from the inside out.[19] In both procedures, the adjustment of the sling under the mid urethra was done by pulling from the inside out. The cure rates on both procedures were not different and, more importantly, they were not different from retropubically placed TVT.[20] The physical and clinical equivalence of the TVT-O, compared to TVT, was demonstrated in a randomized equivalence trial. The overall number of serious adverse events, voiding dysfunction, bladder perforation, and urinary tract infections were more common after the placement of retropubic sling in comparison with the TVT-O. Leg weakness and groin numbness was more frequent after the TVT-O procedure but required no intervention.[21] Complication rates from TVT-O were lower than TVT. There was some early postoperative pain because of the insertion needle path through the superficial muscles of the leg, and several long-term TVT-O studies showed low rates of complications including leg pain and exposure.[22] Five-year, multicenter, randomized control trial comparing TVT and TVT-O high cure rates and patient satisfactions were seen in both. The objective cure rate was 84.7% of the TVT group and 86.2% in the TVT-O group. Subjective treatment satisfaction was higher in both groups as well. Additionally, 84% of patients were cured of their preoperative urgency symptoms. Complication rates were low with no difference between groups and none of the patients had any sign of tissue action,

[19] De Leval J, Novel Surgical Technique for the Treatment of Female Stress Urinary Incontinence: Transobturator Vaginal Tape Inside-Out. Eur Urol 2003;44:724-30; ETH.MESH.00823793.

[20] Palva K, A randomized trial comparing tension-free vaginal tape with tension-free vaginal tape-obturator: 36-month results. Int Urogynecol J 2010;21:1049-55; Sung VW, et al., Comparison of retropubic vs transobturator approach to midurethral slings: a systematic review and meta-analysis. Am J Obstet Gynecol 2007 Jul;197(1):3-11.

[21] Richter HE, Retropubic versus Transobturator Midurethral Slings for Stress Incontinence. N Eng J Med. 2010;362:22:2066-76.

[22] Thomas, Lega, DiCarlo, *International Urogynecology* (2015)

erosion, or tape protrusion at their 5-year followup.[23] Overall, TVT and TVT-O are safe and effective options for the treatment of stress urinary incontinence. There is data as recent as 2016 that shows the safety and efficacy of retropubic midurethral sling placement.[24]

Several long-term studies support the safety and efficacy of the TVT-O. Angioli reported a 72.9% cure rate in their five-year follow-up randomized controlled trial, with low complication rates (3 erosions, and dyspareunia rate 3%).[25] Groutz reported in a five-year prospective study of TVT-O patients that 74% of the patients had their SUI cured, with an additional 8% improved. 2.7% of the patients had residual pain, and there were only two instances of vaginal erosion.[26] Liapis reported an objective cure rate of 80.5% of patients undergoing both a TVT-O and an anterior colporrhaphy, and in 82.4% of the patients receiving only a TVT-O.[27] Serati reported on a five-year follow-up multi-center prospective study and noted a subjective cure rate of 90.3% and an objective cure rate of 90.8%. One patient needed revision surgery for early post-operative voiding dysfunction, and two women had vaginal erosion at one year post-op. By one-month post-op, only 3.1% of the patients had groin pain, and by one year, only 1% did.[28] Laurikainen reported on a five-year follow-up multi-center randomized controlled trial that

[23] Laurikinen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109-14.
[24] Anderson, Blake, *Urology 91* (2016)
[25] Angioli R, et al., Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective Randomised Trial. Eur Urol 2010;58:671–77.
[26] Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. J Women's Health 2011;20(10): 1525–28.
[27] Liapis A, et al., Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. Eur J Obstet Gynecol Reprod Biol 2010;148:199–201.
[28] Serati M, et al., TVT-O for the Treatment of Pure Urodynamic Stress Incontinence: Efficacy, Adverse Effects, and Prognostic Factors at 5-Year Follow-up. Eur Urol 2013;63:872–78.

86.2% of the TVT-O patients and 84.7% of the TVT patients were objectively cured and 91.7% of the TVT-O patients and 94.2% of the TVT patients were subjectively satisfied with their surgery. Both the TVT and TVT-O patients had a significant improvement in quality of life, and they observed one erosion at one-year post-op. 84% of patients with pre-operative urgency symptoms were cured of those symptoms after the procedure, and de novo overactive bladder occurred in 2.4% of the TVT-O patients and 3.1% of the TVT patients after the procedure.[29] Athanasiou reported on seven-year data from a retrospective study of 124 patients receiving TVT-O, and noted an 81.5% and 83.5% objective and subjective cure rate, respectively. There was a 0.8% vaginal erosion rate, a 7% de novo urgency rate, and a 0.8% post-op voiding difficulty rate. There was no groin pain.[30] In 2017, Serati published the ten-year follow-up results of the study, and found no significant change of the surgical outcomes. 97% of the patients declared themselves cured, and 92% of them were objectively cured. 14% had de novo over-active bladder at ten-year follow-up.[31]

3. The TVT-Abbrevo

The TVT-Abbrevo is a shorter (12 cm) version of the full-length TVT-O sling. It is made of the same macroporous, lightweight, knitted, monofilament Prolene mesh that the TVT and TVT-O devices are made of, and the mesh is laser-cut. The TVT-Abbrevo procedure involves reduced depth of lateral dissection, as the obturator membrane is not perforated with the scissors and winged guide. Ethicon

[29] Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109-14.
[30] Athanasiou S, et al., Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail? Int Urogynecol J 2014 Feb;25(2):219-25.
[31] Serati M, et al., Tension-free Vaginal Tape-Obturator for Treatment of Pure Urodynamic Stress Urinary Incontinence: Efficacy and Adverse Effects at 10-year Follow-up. Eur Urol 2017 Apr;71(4):674-9.

developed the TVT-Abbrevo following feedback from surgeons who desired an even less invasive technique than the TVT-O and to reduce potential complications even further. Studies have shown that the TVT-Abbrevo decreases groin pain in the immediate post-operative period and lessens morbidity.[32] Capobianco reported an objective cure rate of 76.79% at one-ear follow-up, with 17.86% more considerably improved. 76.79% were also subjectively cured. No erosions were reported, nor was any persistent groin pain.[33] Shaw reported a statistically significant reduction in groin pain in the TVT-Abbrevo cohort compared to the TVT-O cohort.[34] Tommaselli reported an objective cure rate in a retrospective study of both overweight and normal weight patients receiving a TVT-Abbrevo. They found that approximately 95% of the patients were objectively cured, and 88-90% were subjectively cured, with significant quality of life improvements.[35] Kurien reported in September 2016 the results of a 22-month prospective cohort study and noted a one-year subjective cure rate of 90.6% and an 88.9% improvement or cure rate in the nine patients who completed two-year follow-up.

[32] Tommaselli GA, et al., Comparison of TVT-O and TVT-Abbrevo for the Surgical Management of Female Stress Urinary Incontinence: a 12-Months Preliminary Study. Int J Gynecol & Obstet 119S3 (2012) S261-S530, S504 (Abstract); Waltregny D, et al., New Surgical Technique for Treatment of Stress Urinary Incontinence TVT –ABBREVO: From Development to Clinical Experience. Surg Technol Int. 2012 Dec;22:149-157.

[33] Capobianco G, Dessole M, Lutzoni R, Surico D, Ambrosini G, Dessole S. TVT-ABBREVO: efficacy and two years follow-up for the treatment of stress urinary incontinence. Clin Exp Obstet Gynecol. 2014;41(4):445-7.

[34] Shaw JS, Jeppson PC, Rardin CR, Decreasing transobturator sling groin pain without decreasing efficacy using TVT-Abbrevo. Int Urogynecol J. 2015 Sep;26(9):1369-72. doi: 10.1007/s00192-015-2718-5. Epub 2015 Jun 2.

[35] Tommaselli GA, Napolitano V, Di Carlo C, Formisano C, Fabozzi A, Nappi C, Efficacy and safety of the trans-obturator TVT-Abbrevo device in normal weight compared to overweight patients affected by stress urinary incontinence. Eur J Obstet Gynecol Reprod Biol. 2016 Feb;197:116-9. doi: 10.1016/j.ejogrb.2015.11.014. Epub 2015 Nov 27.

4.5% had a small asymptomatic vaginal erosion at six-months post-op, but there were none at one-year follow-up.[36]

4. TVT-Exact

The TVT-Exact is a full-length retropubic sling that utilizes the same knitted, monofilament, macroporous, lightweight Prolene polypropylene mesh used in the other TVT devices. It is only available in laser-cut mesh. The trocars of the TVT-Exact are slightly thinner and longer than those in the TVT. The studies I have discussed in this report noting the safety and efficacy of the TVT support the safety of the TVT-Exact, as the devices utilize the same mesh, are implanted in the same manner, and support the midurethra the same way, in the same anatomic location. In 2016, Thubert published a retrospective, non-randomized study comparing outcomes in patients receiving the TVT and TVT-Exact slings. They found no statistically significant difference in the rate of bladder perforation between the two slings. They found that the TVT-Exact patients had less intense pain in the immediate post-operative period. They also found more bladder outlet obstruction in the TVT-Exact patients, but when they looked at only de novo bladder outlet obstruction, they did not detect a difference between the TVT and TVT-Exact outcomes. The complications experienced by the patients in the two groups did not statistically significantly differ.[37] In 2015, Aniuliene published a study comparing the TVT-Exact and the SLING-IUFT procedures. In that prospective randomized trial, they found that the TVT-Exact was more effective than the SLING-IUFT procedure. The TVT-Exact was effective in treating the

[36] Kurien A, Narang S, Han HC, Tension-free vaginal tape-Abbrevo procedure for female stress urinary incontinence: a prospective analysis over 22 months. Singapore Med J. 2016 Sep 9. doi: 10.11622/smedj.2016149. [Epub ahead of print].

[37] Thubert T, Canel V, Vinchant M, et al., Bladder injury and success rates following retropubic mid-urethral sling: TVT EXACT™ vs. TVT™. Eur J Obstet & Gynecol and Reprod Biol. 2016 Mar;198:78-83.

TVT-Exact patients' incontinence in 94.5% of the cases, while only the SLING-IUFT was effective in only 61.2% of the patients receiving that device. There was more post-operative urinary retention in the TVT-Exact patients, but more groin pain in the SLING-IUFT patients. Vaginal erosion occurred in 0% of the TVT-Exact patients and in 1.3% of the SLING-IUFT patients.[38]

In 2015, Ford and colleagues published a Cochrane Review on mid-urethral sling operations in women. They analyzed randomized or quasi-randomized controlled trials in which both trial arms involved a midurethral sling, including 81 trials that evaluated 12,113 women. They concluded: "Mid-urethral sling operations has been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI." They found that there is "moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of the tapes." They observed an overall rate of vaginal tape erosion/exposure/extrusion of 2.4% in transobturator sling patients and 2.1% in retropubic sling patients, and that tape erosion was more common in the multifilament tapes than it was in monofilament tapes like those in the TVT family of slings. The average rate of groin pain was 4.51% and both groin and suprapubic pain were short lasting. In all trials there was significant improvement in sexual function compared to before the surgery, and at 24-month

[38] Aniuliene R, Aniulis P, Skaudickas D, TVT-Exact and midurethral sling (SLING-IUFT) operative procedures: a randomized study. Open Med. 2015;10:311-317.

follow-up, rates of superficial and deep dyspareunia were low, with no difference between the transobturator and retropubic sling patients. They also noted that Type 1 mesh has the highest biocompatibility with the least propensity for infection, and that macroporous meshes with pore size in excess of 75 µm easily allow macrophages, leukocytes, fibroblasts, blood vessels and collagen to transverse the pores, thereby promoting tissue host ingrowth with resultant biocompatibility and low risk of infection.[39]

Tommaselli and colleagues published a systematic review and meta-analysis of medium- and long-term outcomes following midurethral sling surgery. They reported that retropubic slings had similar objective cure rates to transobturator slings, but higher subjective cure rates. They reported that 13 out of 3,974 (0.3%) retropubic patients had persistent or chronic pain, and 30 out of 2,432 (1.2%) transobturator patients did.[40]

In 2014, the Society of Gynecologic Surgeons Systematic Review Group published a systematic review and meta-analysis of randomized controlled trials with a minimum of one year of follow-up comparing a sling procedure to another sling procedure or a Burch procedure. Table 3 of the study shows the rates of various adverse events with transobturator slings like the TVT-O and TVT-Abbrevo, with retropubic slings like the TVT and TVT-Exact, with minislings, with the Burch procedure, and with pubovaginal slings. The study shows that the complication rates seen with midurethral slings compares very favorably with the Burch

[39] Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375.DOI: 10.1002/14651858.CD006375.pub3.

[40] Tommaselli GA, Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015 Sep;26(9):1253-68.

procedure or with pubovaginal sling procedures. The authors suggested either midurethral slings or the Burch procedure for treatment of SUI based on cure rates, with the decision to be based on which adverse events are of greatest concern to the patient and whether any concomitant surgeries are planned. For women considering either a pubovaginal sling or the TVT midurethral sling, the authors recommended the TVT for better cure rates.[41]

In 2009, Ogah and colleagues published a Cochrane Review regarding outcomes of synthetic midurethral sling patients. They found that monofilament tapes had significantly higher objective cure rates compared to multifilament tapes and fewer tape erosions, and that for retropubic slings, a bottom-to-top approach was more effective than a top-to-bottom approach, with the former resulting in significantly less voiding dysfunction, bladder perforations, and tape erosions. They found that midurethral sling procedures were as effective as pubovaginal slings, but had shorter operating time and less post-operative voiding dysfunction and de novo urgency. They also observed that midurethral sling surgeries were as effective as open retropubic colposuspension (the Burch procedure), but with fewer perioperative complications, less postoperative voiding dysfunction, shorter operative time, and hospital stay, but significantly more bladder perforations. The authors concluded that midurethral sling operations are "as effective as traditional suburethral slings, open retropubic colposuspension and laparoscopic colposuspension in the short term but with less postoperative complications."[42]

[41] Schimpf MO, et al. Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014 Jul;211(1):71.e1-71.e27. doi: 10.1016/j.ajog.2014.01.030. Epub 2014 Jan 30.

[42] Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD006375. DOI: 10.1002/14651858.CD006375.pub2.

In 2011, Ogah and colleagues published a short version Cochrane Review that analyzed 62 studies involving 7,101 women. They found that minimally invasive synthetic midurethral sling surgery appeared to be as effective as traditional suburethral slings, but with shorter operative time and less postoperative voiding dysfunction and de novo urgency symptoms. They were also as effective as open retropubic colposuspension with fewer perioperative complications, less postoperative voiding dysfunction, shorter operative time, and hospital stay, but with more bladder perforations. They also noted that monofilament tapes had significantly higher objective cure rates than multifilament tapes, with fewer mesh erosions.[43]

Jonsson-Funk and colleagues conducted a population-based cohort study of commercially insured individuals who underwent a midurethral sling procedure and any subsequent sling revision or removal. 188,454 women who underwent a sling were included in the study, and the authors found the nine-year cumulative risk of sling revision or removal was 3.7%. The nine-year risk for undergoing a revision surgery for mesh erosion was 2.5%, and for urinary retention it was 1.3%.[44]

Unger and colleagues reported the results of their case-control study of all women who received a midurethral sling for SUI between January 2003 and December 2013. Cases were patients receiving a midurethral sling placement followed by a sling revision, and controls were patients receiving a midurethral sling without a subsequent revision. In all, 3,307 women underwent sling placement, and 2.7%

[43] Ogah J, et al., Minimally Invasive Synthetic Suburethral Sling Operations for Stress Urinary Incontinence in Women: A Short Version Cochrane Review. Neurourol Urodyn 2011;30:284-91.
[44] Jonsson Funk M, Siddiqui NY, Pate V, Amundsen CL, Wu JM, Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors. Am J Obstet Gynecol 2013; 208:73.e1-7.

underwent sling revision for one or more of the following: urinary retention, voiding dysfunction, recurrent urinary tract infection, mesh erosion, vaginal pain/dyspareunia, and groin pain. Out of the 3,307 women, 0.2% of the women had a revision for vaginal pain/dyspareunia, 0.09% for groin pain, 0.6% for mesh erosion, 1.2% for urinary retention, and 1.1% for voiding dysfunction. The overall rate of sling revision after midurethral sling placement was 2.7%. There was no association between one type of sling versus another (retropubic vs. transobturator) and the need for sling revision.[45]

Welk and colleagues conducted a population-based retrospective cohort study that included all adult women who had a synthetic mesh sling implant for treatment of SUI in Ontario, Canada from April 1, 2002 through December 31, 2012—a total of 59,887 patients. They found that the ten-year cumulative incidence of complications was 3.29%. They also noted that, in the majority of cases, the revision surgery was performed by the surgeon who performed the index procedure.[46]

Drs. Ashley Cox, Sender Herschorn, and Livia Lee published a review of the literature regarding stress urinary incontinence treatment in 2013, and concluded that, "based on the literature, however, a new gold standard first line surgical treatment for women with SUI has emerged—the synthetic midurethral sling inserted via a retropubic or transobturator approach."

[45] Unger CA, Rizzo AE, Ridgeway B, Indications and risk factors for midurethral sling revision. Int Urogynecol J 2016 Jan;27(1):117-22. doi: 10.1007/s00192-015-2769-7. Epub 2015 Jul 2.
[46] Welk B, Al-Hothi H, Winick-Ng J, Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence. JAMA Surg. 2015 Dec;150(12):1167-75. doi: 10.1001;jamasurg.2015.2590.

Nguyen and colleagues published the results of their study of all female members of Kaiser Permanente Southern and Northern California and Hawaii who underwent sling procedures or pelvic organ prolapse surgeries with implanted grafts or mesh between September 1, 2008 and May 31, 2010. Out of 3,747 women undergoing sling procedures, bladder perforation occurred in 1.4% of cases, and urethral perforations occurred in 0.05% of cases. Mesh-related re-operations occurred for urinary retention in 1.3% of patients, for mesh erosion in 0.8% of patients, and for urethral erosion in 0.08% of patients.[47]

Numerous professional societies and organizations have endorsed the use of midurethral slings like the TVT, TVT-Exact, TVT-O, and TVT-Abbrevo. In 2014, the American Urogynecologic Soceity (AUGS) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) issued a Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence. In that position statement, they observed: "The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women." They noted that polypropylene is safe and effective as a surgical implant, has been used in most surgical specialties for over 50 years in millions of patients in the United States and the world. They also observed that the monofilament polypropylene mesh midurethral sling is the most extensively studied anti-incontinence procedure in history, and that "a broad evidence base including high quality scientific papers in medical journals in the US and the world supports the use of the MUS as a treatment for SUI." "No other surgical treatment for SUI before or since has been subject to such extensive

[47] Nguyen JN, Jakus-Waldman SM, Walter AJ, White T, Menefee SA, Perioperative Complications and Reoperations After Incontinence and Prolapse Surgeries Using Prosthetic Implants. Obstet Gynecol 2012 Mar;119(3):539–46.

investigation." They concluded: "The polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly."[48] The position statement was updated in 2016, and was supported by the American Association of Gynecological Laparoscopists (AAGL), the American College of Obstetricians and Gynecologists (ACOG), the National Association for Continence (NAFC), the Society of Gynecologic Surgeons (SGS), and the Women's Health Foundation (WHF).

The American Urological Association issued its own position statement on the use of vaginal mesh for the surgical treatment of SUI, and noted that "it is the AUA's opinion that any restriction of the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI."[49] ACOG and AUGS issued a practice bulletin on urinary incontinence in women in November 2015, which noted that synthetic suburethral slings are similarly effective to traditional suburethral fascial slings or the Burch procedure, and compared to suburethral fascial slings, they have fewer adverse events. Midurethral slings were also noted to have less voiding dysfunction than open Burch procedures.[50]

The International Urogynecological Association issued its Position Statement on Mid-Urethral Slings for Stress Urinary Incontinence in July 2014. In the statement, IUGA noted that it "supports the use of monofilament polypropylene mid-urethral slings for the surgical treatment of female stress urinary incontinence." IUGA also noted that "there is robust evidence to support the use

[48] AUGS & SUFU Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence 2014.
[49] AUA Position Statement on the U
[50] ACOG & AUGS, Urinary Incontinence in Women, Practice Bulletin Summary No. 155, Nov. 2015.

of MUS from over 2,000 publications making this treatment the most extensively reviewed and evaluated procedure for female stress urinary incontinence now in use."[51]

In 2015, the International Continence Society issued a fact sheet on incontinence, which noted that "worldwide, midurethral slings comprised of synthetic mesh have become the treatment of choice for SUI. Long-term data are robust and demonstrate durable efficacy with a very low complication rate, particularly in experienced hands."[52]

IV. RESPONSE TO PLAINTIFF'S CONTENTIONS RE: ALLEGED DESIGN DEFECTS

The clinical data demonstrates that the knitted, monofilament, lightweight, macroporous Prolene polypropylene mesh used in the TVT, TVT-O, TVT-Abbrevo, and TVT-Exact slings is biocompatible, has a minimal inflammatory response, and allows for adequate tissue growth, the mechanism by which mesh ultimately provides the necessary structural support in women with stress urinary incontinence. This data also shows that Ethicon's mesh is not associated with significantly increased risks of infection over that of generally associated risk for vaginal surgery. There is no published data that suggests the mesh in the slings is cytotoxic or causes adverse inflammatory response, sarcoma, or cancer. By the sheer numbers of women in whom the slings were implanted, if there was merit to a claim of cytotoxicity, you would certainly expect valid data to demonstrate that claim in replicable studies. Similarly, there is no reliable data to support any claim that the manner in which the mesh is trimmed or cut (whether mechanically or laser cut) has any clinical relevance or significance. Reliable data does not support that the mesh degrades or loses particles in situ, and if there was some loss, the clinical significance is not demonstrated. The mechanically and laser cut TVT and TVT-O were within the

[51] IUGA Position Statement on Mid-Urethral Slings for Stress Urinary Incontinence 2014.
[52] ICS Fact Sheet—A Background to Urinary and Faecal Incontinence, 2015.

standard of care and none of the pertinent SUI guidelines and analysis distinguish efficacy or safety of the device based on the way the edges of the mesh are cut nor do they support the theory espoused by the plaintiff's expert.

When the mesh is removed as an explant from patients, it is exposed to forces well beyond the intended force for a sling and prolapse procedure. Therefore, the change from an explanted mesh is different than a host graft interaction because the act of explanting changes the mesh as it is removed from the patient. It has no predictive value. Prolene polypropylene has been used in millions of sutures, slings, and Gynemesh PS. A Medline search for sarcoma in polypropylene does not yield a single case of sarcoma or malignancy due to the use of polypropylene materials in humans. MSDS and rat studies reporting sarcoma formation after implantation of polypropylene discs and powder are not transferrable to humans.[53] The available data does not show any causal link between polypropylene and cancer.[54] As observed by AUGS and SUFU in their 2014 Frequently Asked Questions by Providers on mid-urethral sling for SUI, their response is as follows. "Tumors related to the implantation of surgical grade polypropylene for mid-urethral slings in humans have never been reported. There is no compelling evidence supporting the human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material spanning well over half a century worldwide. The possibility of the biomaterial prosthetic devices could cause tumors or prolonged tumor growth has been the focus of extensive research by both clinicians and biomaterial researchers. There is no reliable evidence of human

[53] King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453.
[54] Moalli P, et al., Polypropylene mesh: evidence for lack of carcinogenicity. Int Urogynecol J. 2014 May;25(5):573-6; March 12, 2014, AUGS SUFU Frequently Asked Questions; King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J. 2016 Sep;27(9):1333-6.

cytotoxicity. One cytotoxicity assessment of the TVT sling (made of Prolene polypropylene) in 1997 indicated the polypropylene may have cytotoxic potential;[55] however, this was not confirmed by the ISO Agarose diffuse method.[56] And the company correctly recognized that the assessment of the biocompatibility of the material had to take into consideration all available data, including clinical data, and when doing so, it was apparent that the Prolene materials did not have any clinically significant cytotoxicity translating to adverse patient outcomes.[57] Cytotoxicity assessment of the Ulmsten Prolene polypropylene sling using the ISO elution method showed cell lysis and toxicity; however, this was not confirmed by the ISO Agarose diffuse method.[58] Normal production of Prolene polypropylene has not shown any cytotoxicity at drug elution, ISO Agarose overlay method, or with extraction/filter paper method. All testing methods used monolayer of L-929 mouse fibroblast cells.[59] There are five decades of use of polypropylene mesh implants, and it is a stable, well-accepted biomaterial.[60]

In recent years, there have been concerns regarding polypropylene degradation by high-magnification images that show meshes with "cracked" surfaces.[61] In the Clavé study, there were many methodological flaws. While these purported surface changes were hypothesized to lead to adverse clinical outcomes, they cannot be confirmed, and there is no extensive peer review literature that supports this hypothesis. There are studies that suggest clinically significant mesh degradation occurs, but there are other studies that indicate that the surface cracking interpreted by some as being evidence of mesh

[55] ETH.MESH.08476311.
[56] ETH.MESH.08476314.
[57] C. Linsky memo re Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device, ETH.MESH.00349228.
[58] ETH.MESH.08476311; ETH.MESH.08476314
[59] ETH.MESH08476315-6.
[60] AUGS/SUVU SUFU Facts by Providers, Urogynecology (March 2010).
[61] Clavé A, et al., Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. Int Urogynecol J 2010;21:261-270.

degradation is actually cracking in a biofilm overlying the polypropylene.[62] Based on my positive experience using the slings in my patients and on my reading of the published literature, it is my opinion that clinically significant mesh degradation does not occur with Ethicon's products. The large volume of medical literature, which includes over 100 randomized controlled trials regarding the TVT alone, metaanalysis, and systematic reviews, does not support that the mesh is cytotoxic, that it degrades, or leads to harmful inflammatory responses in humans. Actually, the use of macroporous type 1 Prolene polypropylene has been shown to be the most biocompatible material for the use and treatment of POP with high- level clinical data. Overall, the data shows that the TVT, TVT-Exact, TVT-O, and TVT-Abbrevo are safe and effective. They are not defective, and these incredibly studied devices are quite useful in the approach to repairing and resolving stress urinary incontinence.

Mesh shrinkage or contraction is discussed in the literature, but is somewhat of a misnomer. Scar tissue does shrink or contract during the healing process, and the scar tissue that is incorporated into the sling devices is no exception, but the mesh itself does not contract or shrink. Scar tissue that forms following native tissue repairs or implantation of biologic graft materials also shrinks and contracts.

Finally, it is my opinion that the data does not support the theories that mesh is cytotoxic, that it degrades or causes harmful inflammatory response, that the pore size, weight, and other features are harmful or cause significant detrimental clinical outcomes. The pore size of the products is far in excess of the 75-micron threshold widely recognized to constitute a macroporous mesh, and allows for excellent tissue ingrowth and very low rates of infection. While there is no agreed-upon classification system for the weight or

[62] Ong KL, et al., The Myth: In Vivo Degradation of Polypropylene Meshes. IUGA 2016, Abs. PP 19; de Tayrac R and Letouzey V, Basic science and clinical aspects of mesh infection in pelvic floor reconstructive surgery. Int Urogynecol J 2011 Jul;22(7):775-80.

density of meshes, the mesh used in the TVT family of products addressed in this report is lightweight mesh. Ethicon studied these products more than any other company in this surgical arena and more than adequately trained the physicians that performed the surgery. Ethicon also kept these physicians well informed of all the data as it was collected, both supportive and critical.

V. TVT AND TVT-O INFORMATION PROVIDED TO PHYSICIANS

A. Each TVT and TVT-O device is accompanied by an IFU (instructions for use). I have reviewed the TVT, TVT-Exact, TVT-Abbrevo, and TVT-O IFUs and find them adequate and complete for its use by the intended users—pelvic reconstructive surgeons. It is clear that an IFU is not a comprehensive guide for the surgical treatment of stress urinary incontinence. The IFU builds on the knowledge that we as pelvic floor surgeons have acquired through our prior education, instruction, and experience. These materials are important, but as I know in my training and in the training of other surgeons, these IFUs are by no means our primary means of learning about the products or the surgery itself. We learn how to perform these surgeries and the use of mesh with its proper application in our residencies, fellowships, and proctorships. We rely on published medical articles, presentations at professional meetings, and discussions with colleagues as well as live surgery and cadaver labs, which are provided by the drug manufacturers. Ethicon, by far, did the best training regarding the use of these mesh products and educating its surgeons regarding stress incontinence, pelvic organ prolapse, and providing more than adequate data and resources so the surgeons could make informed decisions regarding the type of procedure and the products that they wish to use. The IFUs did list several risks including damage to vessels, nerves, bladder and bowel inflammation, extrusion, and erosion. However, any surgeon practicing pelvic reconstructive surgery understands that these complications may cause pain and dyspareunia as well as the need for additional surgery. It was not necessary for the IFU to reiterate potential postop commonly

known complications. In 2008, the FDA published a pelvic health notice concerning surgical pelvic mesh. This public health notice discussed both potential complications and counseling of patients. In 2013, the FDA published an updated notice concerning the SUI meshes like TVT and TVT-O which was titled *Considerations About Surgical Mesh for SUI*. This notice identifies the safety and effectiveness of multi-incision slings, like TVT and TVT-O, is well established in clinical trials that follow patients for up to 1 year and that longer followup data is available in the literature. There are hundreds of clinical studies, randomized controlled trials, systemic reviews and metaanalysis, and clinical guidelines including numerous studies with durations of 5, 10, and 15 years that have been published and are widely available to all surgeons. The FDA correctly observed that, apart from mesh exposure, these complications can occur following a non-mesh surgical repair for SUI. These risks associated with incontinence surgeries are commonly known among pelvic floor surgeons, and in my opinion, do not need to be individually itemized in the IFUs of the products. It is neither helpful nor necessary, in my opinion, for device IFUs to list risks that are commonly known. Furthermore, surgeons know that any complications that occur following a surgery can be temporary or permanent, and they can be mild, moderate or severe. It is not necessary for an IFU to provide that information. Nor is it necessary for the IFU to specify the frequency with which various complications occur. Those rates are published in the medical literature that surgeons regularly review; they vary significantly in some instances, and are often changing. The treatment of complications following mesh implantation surgery is something that surgeons learn in residency and fellowship, and something surgeons know how to do based on their familiarity with the female anatomy and their training.

B. The company's patient brochures are excellent, and I use them in my practice as part of my counseling of patients. They are updated frequently and include the FDA warnings as mentioned above. These brochures do not replace the informed consent process, but it is an excellent resource for additional information and the possible

complications inherent to incontinence procedures. Ethicon's professional education material and training were most helpful in informing physicians of the proper use and risk of its products. It is my opinion that Ethicon went above and beyond to educate, train, and facilitate the surgical approach to stress urinary incontinence. Their training was exceptional, their products were studied thoroughly, and there was not another company in this arena that came close in educating and providing the tools needed for a surgeon to use these products. The pertinent societies continue to analyze the voluminous data which support TVT and TVT-O. The November 2015 ACOG and AUGS Practice Bulletin 155 Urinary Incontinence in Women recommend the TVT and the TVT-O because they are safe and effective and less invasive and morbid than alternatives.[63] The following conclusions are recommendations with which I agree were determined to be based on good, consistent scientific evidence (level A).

- Initial mid-urethral sling surgery results in higher one-year subjective and objective cure rates the pelvic floor physical therapy in women with stress incontinence.
- Synthetic mid-urethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension. Compared with the suburethral fascial slings, fewer adverse events have been reported with synthetic material mid-urethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic mid-urethral slings.
- There is substantial safety and efficacy data that support the role of synthetic mesh mid-urethral slings as a primary surgical treatment option for stress urinary incontinence in women.
- Burch colposuspension at the time of abdominal sacral colpopexy and retropubic mid-urethral sling at the time of vaginal surgery for pelvic organ

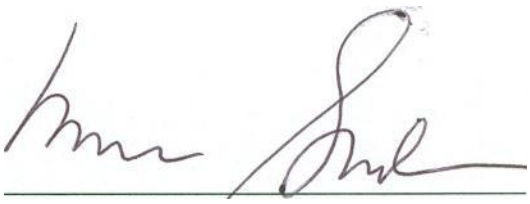
[63] Committee Packet Bulletins *American College of OB-GYN* (November 2015)

prolapse repair decrease the risk of postoperative stress urinary incontinence in women without preoperative stress urinary incontinence.

Lastly, it is my opinion TVT and TVT-O are safe and effective within the standard of care and are suitable first-line surgical options with more support in medical literature than any other mid-urethral slings.[64] The TVT and TVT-O devices are not defective, and they have significant usefulness to surgeons. The data does not support that the TVT and TVT-O are cytotoxic; that they degrade or cause harmful inflammatory responses; and that their porous, size, weight, mechanical or laser cut or other features were harmful or cause significant clinical outcomes.

The opinions reflected in this report are based on information currently available to me. I reserve the right to modify or amend these opinions as new information becomes available.

Dated: June 1, 2017



Marshall Shoemaker, M.D.

[64] *Cochrane Review* (February 2, 2015); AUGS FU Statement (2014); ACOG Statement (2014); IUGA Statement (2014); SGS Guidelines (2014); AUA Position Statement (2013); Nice Clinical Guideline 171 (2013); ICSSU Fact Sheet (2013); EAU Guideline (2012); AUA Guideline (2012); Cox Review (2013); Cochrane Review (2011); Navarre Metaanalysis (2010)